

FDA Updates on Biological Product Naming

Kellie Taylor

Lonnie Smith

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Background



- The Biologics Price Competition and Innovation Act of 2009 (BPCI Act) was passed by Congress in 2009 and signed into law in 2010 to create an abbreviated licensure pathway for biological products shown to be biosimilar to or interchangeable with an FDA-licensed reference product.
- BPCI Act creates an ***abbreviated licensure pathway for biological products shown to be biosimilar to or interchangeable with*** an FDA-licensed reference product.

What is an Abbreviated Licensure Pathway for Biological Products?



- A biological product that is demonstrated to be biosimilar to or interchangeable with an FDA-licensed reference product may rely for licensure on, among other things, publicly-available information regarding FDA's previous determination that the reference product is safe, pure and potent.
- This abbreviated licensure pathway under section 351(k) of the PHS Act permits a biosimilar or interchangeable product to be licensed based on less than a full complement of product-specific preclinical and clinical data.

Terms

Reference Product

- the single biological product, licensed under section 351(a) of the PHS Act, against which a biological product is evaluated in an application submitted under section 351(k) of the PHS Act.

Biosimilar or Biosimilarity

- the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and
- there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.

Terms (Cont.)

Interchangeable or Interchangeability :

- the biological product is **biosimilar** to the reference product;
- it can be expected to produce the **same clinical result** as the reference product **in any given patient**; and
- for a product that is administered more than once to an individual, the risk in terms of **safety or diminished efficacy of alternating or switching** between use of the product and its reference product is not greater than the risk of using the reference product without such alternation or switch.

Under the BPCI Act, an interchangeable product **may be substituted** for the reference product without the intervention of the health care provider who prescribed the reference product.

Related Biological product (see FDA Naming Guidance):

- a biological product submitted in a BLA under section 351(a) (i.e., a stand-alone BLA);
- For which there is a previously licensed biological product submitted in a different section 351(a) BLA that contains a drug substance for which certain nomenclature conventions (e.g. United States Adopted Names (USAN) Guiding Principles) would be expected to provide for use of the same drug substance name.
 - Example: tbo-filgrastim

Biological Product Naming Development

- The Biologics Price Competition and Innovation Act of 2009 (BPCI Act) created an approval pathway for biological products shown to be biosimilar to or interchangeable with an FDA-licensed biological reference product.
- As part of FDA's implementation of the BPCI Act, FDA requested public comment in public meetings held in 2010 and 2012 on its development of a framework for safe use and optimal pharmacovigilance for biosimilar products and interchangeable products, including the role of a product's nonproprietary name.
- In August 2015, FDA published the draft guidance *Nonproprietary Naming of Biological Products*. FDA published the final version of this guidance in January 2017. The guidance describes FDA's current thinking on the nonproprietary naming convention for biological products licensed under the Public Health Service Act (PHS Act).

Nonproprietary Naming of Biological Products

Final Guidance issued January 2017

1. Nonproprietary names (i.e. proper names) for biological products should include **a core name attached by a hyphen to an FDA-designated suffix that is devoid of meaning** (e.g. infliximab-dyyb).
2. **A unique suffix should be designated for each originator biological product, related biological product and biosimilar product.**
 - FDA is continuing to consider the format of the suffix for interchangeable biological products.
3. **The naming convention applies to all products, prospectively and retrospectively.**
 - FDA is continuing to consider the process for implementing this naming convention for previously licensed products.

Naming Convention: Objectives

Transparency:

- Allows identification of products for safe use and pharmacovigilance
- Facilitates prescribing and dispensing of the intended product
- Patients and providers want to know what the patient received

Trust:

- Practitioners and patients want FDA and others to have the tools available to perform product-specific pharmacovigilance in all settings of care

Uptake:

- Enhanced prescriber and public confidence facilitates market uptake

Nonproprietary Naming: 351(a) AND 351(k)

- Application of the naming convention to *originator* and *related* biological products (351(a) BLAs) and *biosimilar* products (351(k) BLAs)
 - encourages routine use of designated suffixes in ordering, prescribing, dispensing, and recordkeeping and
 - avoids inaccurate perceptions of the safety and effectiveness of biological products based on their licensure pathway.

Nonproprietary Naming: Examples

- For example, for hypothetical products sharing the fictitious core name *replicamab*, the proper names would include a unique suffix:
 - Originator biological product : *replicamab-cznm*
 - Related biological product: *replicamab-rzbh*
 - Biosimilar product: *replicamab-hixf*
- FDA has approved 6 biosimilars
 - Zarxio (filgrastim-sndz), biosimilar to Neupogen
 - Inflectra (infliximab-dyyb), biosimilar to Remicade
 - Erelzi (etanercept-szzs), biosimilar to Enbrel
 - Amjevita (adalimumab-atto), biosimilar to Humira
 - Renflexis (infliximab-abda), biosimilar to Remicade
 - Cyletezo (adalimumab-adbm), biosimilar to Humira

Nonproprietary Naming: Retrospective

- ***FDA is continuing to consider the process for implementing the naming convention for previously licensed products.***
- In August 2015, FDA issued a proposed rule to modify the nonproprietary name of six currently marketed biological products.
- Commenters expressed concern about potential costs associated with changing the nonproprietary names of currently marketed biological products. FDA will continue working with stakeholders, including manufacturers, health systems and informatics providers, to better understand these costs.
- The final guidance permits BLA holders to propose a suffix for use in the proper name of currently licensed biological products. The process for BLA holders to propose suffixes is part of an information collection subject to OMB review under the Paperwork Reduction Act.

Education And Outreach

FDA has a multi-phase plan for communicating with stakeholders about biosimilars in various formats.

- **Continuing Education (CE) course “FDA Overview of Biosimilar Products”:** released February 2016; target audience is healthcare professionals (e.g., physicians, nurses, and pharmacists).
- **Research and Message Development:** The FDA conducted focus groups and in-depth interviews with HCPs to learn about their perceptions of biosimilar and interchangeable. FDA plans to continue research with prescribers to learn about their experiences communicating with patients; as well as to test educational materials.
- **Current Campaign:** FDA plans to release educational materials for health care prescribers this fall and will continue to disseminate easy-to understand materials on biosimilars in a variety of formats. FDA will begin developing materials for patients in 2018.
- **Purple Book:** The “Purple Book” lists biological products (including biosimilar and interchangeable products) licensed by FDA under the PHS Act.

Indexing – Biological Drug Substance SPL Document

Unique Ingredient Identifier (UNII)



- Scientific identification
 - Think Periodic Table of Elements
- Identification at the substance level (UNII) independent of product/manufacturing information
- Follows ISO Identification of Medicinal Products (IDMP)
 - ISO 11238 Substances/Specified Substances
- Must maintain the integrity of the UNII substance term(s) and identifier

UNII Substance Identification:

Filgrastim

Protein Sequence:

<SEQUENCE>MTPLGPASSLPQSFLKCLEQVRKIQGDGAALQEKLCATYKLCHPEELVLLG
HSLGIPWAPLSSCPSQALQLAGCLSQLHSGFLYQGILLQALEGISPELGPTLDTLQLDVADFA
TTIWQQMEELGMAPALQPTQGAMPAFASAFQRRAGGVLVASHLQSFLEVSYRVLRLHLAQ
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Biological Drug Substance-UNII Substance Relationship

Biological Drug Substance: ICH M4Q(R1)-Module 3: Quality

3.2.S DRUG SUBSTANCE

(NAME, MANUFACTURER)

3.2.S.1 General Information (name, manufacturer)

3.2.S.1.1 Nomenclature (name, manufacturer)

Information on the nomenclature of the drug substance should be provided.

Examples:

Company or laboratory code;

Other non-proprietary name(s), e.g., national name

UNII Substance Identification:

Filgrastim: PVI5M0M1GW

Protein Sequence:

<SEQUENCE>MTPLGPASSLPQSFLKCL
EQVRKIQGDGAALQEKLCAKYKLCHPEE
LVLLGHSLGIPWAPLSSCPSQALQLAGCL
SQLHSGLFLYQGILLQALEGISPELGPTLDT
LQLDVADFATTIWQQMEELGMAPALQP
TQGAMPAFASAFQRRAGGVLVASHLQS
FLEVSRYRLRHLAQP</SEQUENCE>

Biological Drug Substance Category

Proprietary Name	Non-Proprietary Name	Biological Drug Substance (3.2.S)	Substance (UNII)
Neupogen®	filgrastim	filgrastim PVI5M0M1GW-1	filgrastim: PVI5M0M1GW
Zarxio™	filgrastim-sndz	filgrastim-sndz PVI5M0M1GW-SNDZ-1	filgrastim: PVI5M0M1GW
Granix®	tbo-filgrastim	tbo-filgrastim PVI5M0M1GW-TBO-1	filgrastim: PVI5M0M1GW

1. Biological drug substance terms would be associated (not synonyms)
2. Allows each biological drug substance to be uniquely identified
3. Addresses ambiguity with using non-proprietary names as synonyms at the UNII substance level
4. Support the non-proprietary name/biological drug substance relationship throughout the lifecycle.



Biological Drug Substance Indexing SPL

SPL Data Element	XML Code Snippet
Link (set ID) to product's SPL file	<pre><relatedDocument> <setId root="fe707775-a0ae-41b5-a744-28c41889fce8"/> </relatedDocument></pre>
Proprietary Name	<pre><manufacturedProduct> <name>ZARXIO</name></pre>
Substance UNII & Name	<pre><ingredientSubstance> <code code="PVI5M0M1GW" codeSystem="2.16.840.1.113883.4.9"/> <name>filgrastim</name></pre>
Timeframe for use of Biological Drug Substance Name	<pre><code code="48779-3" codeSystem="2.16.840.1.113883.6.1" displayName="SPL indexing data elements section"/> ... <effectiveTime> <low value="20150306"/> <!-- high value="###end-date placeholder###"/ --></pre>

Biological Drug Substance Indexing SPL



SPL Data Element	XML Code Snippet
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Application Type & Number	<pre><subjectOf> <approval> <id extension="BLA125553" root="2.16.840.1.113883.3.150"/> </approval> </subjectOf></pre>
Document Author	<pre><author> <assignedEntity> <representedOrganization> <id root="1.3.6.1.4.1.519.1" extension="927645523"/> <name>Food and Drug Administration</name> </representedOrganization> </assignedEntity> </author></pre>

FDA-to-NLM-to-Healthcare Information Systems



